

Listing of Claims

This listing of the claims will replace all prior versions, and listings, of claims in this application.

1 – 59. (Cancelled)

60. (New) A method of identifying compounds that bind to a leukotriene A₄ (LTA₄) hydrolase, comprising:

- (a) crystallizing a purified LTA₄ hydrolase to form an LTA₄ hydrolase crystal;
- (b) determining the atomic coordinates of said LTA₄ hydrolase crystal; and
- (c) screening the atomic coordinates of a set of candidate compounds against the atomic coordinates of said LTA₄ hydrolase crystal to identify compounds that bind to LTA₄ hydrolase.

61. (New) The method of claim 60, wherein the LTA₄ hydrolase is purified by adsorption chromatography on hydroxyapatite and anion-exchange chromatography.

62. (New) The method of claim 60, wherein the purified LTA₄ hydrolase is crystallized using YbCl₃ as an additive and a complementary compound as a complexing agent.

63. (New) The method of claim 62, wherein said complementary compound is an inhibitor of LTA₄ hydrolase.

64. (New) The method of claim 63, wherein the inhibitor of LTA₄ hydrolase is bestatin, thiolamine or hydroxamic acid.

65. (New) The method of claim 60, wherein the LTA₄ hydrolase has the amino acid sequence set forth in SEQ ID NO. 1.

66. (New) The method of claim 60, wherein said LTA₄ hydrolase comprises an enzymatically active site defined by the following amino acids: Gln136; Ala 137; Tyr267; Gly268; Gly269; Met270; Glu271; Val292; His295; Glu296; His299; Trp315; Glu318; Val322;

Phe362; Val367; Leu369; Pro374; Asp375; Ile372; Ala377; Pro382; Tyr378; Tyr383; Arg563; and Lys565 of SEQ ID NO:1.

67. (New) The method of claim 60, wherein said LTA₄ hydrolase comprises an enzymatically active site defined by the following amino acids: Gln136; Ala137; Tyr267; Gly268; Gly269; Met270; Glu271; Val292; His295; Glu296; His299; Glu318; Tyr378; Tyr383; Arg563; and Lys565 of SEQ ID NO:1.

68. (New) The method of claim 60, wherein the atomic coordinates of said LTA₄ hydrolase crystal correspond to the atomic coordinates defining atom 1 to atom 4876 as set forth in Table 9.

69. (New) The method of claim 60, wherein said LTA₄ hydrolase comprises an enzymatically active site defined by the following amino acids: Lys608, Asp606, Lys605, Lys354, Thr355, Phe356, Phe362, Gln544, Asp573, Lys572, Arg568, Val376, Lys565, Arg540, Leu507, Ser380, Ser352, Glu348, Pro569, Tyr378, Glu348, Arg563, Glu533, Phe536, Arg537, Tyr267, Tyr383, Phe314, Glu318, Glu384, Arg326, Gly268, Gly269, Met270, His295, Asn341, Phe340, Ser288, His497, Glu325 and Asn291 of SEQ ID NO:1.

70. (New) A method of designing an inhibitor or agonist of LTA₄ hydrolase, comprising:

- (a) identifying and/ or synthesizing at least one compound that binds to LTA₄ hydrolase by screening the atomic coordinates of a set of candidate compounds against the atomic coordinates of a purified LTA₄ hydrolase crystal;
- (b) refining the compound identified and/ or synthesized by step (a) by cycles of X-ray crystallography; and
- (c) evaluating the bioactivity of the identified and/or synthesized compound by assessing the activity of LTA₄ hydrolase.

71. (New) The method of claim 70, wherein the LTA₄ hydrolase is purified by adsorption chromatography on hydroxyapatite and anion-exchange chromatography.

72. (New) The method of claim 70, wherein said compound is an inhibitor of LTA₄ hydrolase.

73. (New) The method of claim 70, wherein the LTA₄ hydrolase has the amino acid sequence set forth in SEQ ID NO. 1.

74. (New) The method of claim 70, wherein said LTA₄ hydrolase comprises an enzymatically active site defined by the following amino acids: Gln136; Ala 137; Tyr267; Gly268; Gly269; Met270; Glu271; Val292; His295; Glu296; His299; Trp315; Glu318; Val322; Phe362; Val367; Leu369; Pro374; Asp375; Ile372; Ala377; Pro382; Tyr378; Tyr383; Arg563; and Lys565 of SEQ ID NO:1.

75. (New) The method of claim 70, wherein said LTA₄ hydrolase comprises an enzymatically active site defined by the following amino acids: Gln136; Ala137; Tyr267; Gly268; Gly269; Met270; Glu271; Val292; His295; Glu296; His299; Glu318; Tyr378; Tyr383; Arg563; and Lys565 of SEQ ID NO:1.

76. (New) The method of claim 70, wherein the atomic coordinates of said LTA₄ hydrolase crystal correspond to the atomic coordinates defining atom 1 to atom 4876 as set for in Table 9.

77. (New) The method of claim 70, wherein said LTA₄ hydrolase comprises an enzymatically active site defined by the following amino acids: Lys608, Asp606, Lys605, Lys354, Thr355, Phe356, Phe362, Gln544, Asp573, Lys572, Arg568, Val376, Lys565, Arg540, Leu507, Ser380, Ser352, Glu348, Pro569, Tyr378, Glu348, Arg563, Glu533, Phe536, Arg537, Tyr267, Tyr383, Phe314, Glu318, Glu384, Arg326, Gly268, Gly269, Met270, His295, Asn341, Phe340, Ser288, His497, Glu325 and Asn291 of SEQ ID NO:1.